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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/500,634	01/24/2005	Yoram Sela	SELA=5	3015

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EXAMINER	
VU, JAKE MINH	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)
	10/500,634	SELA, YORAM
	Examiner	Art Unit
	JAKE VU	1618

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 March 2011*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *29-40 and 42-49* is/are pending in the application.

4a) Of the above claim(s) *44 and 45* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19-40,42,43 and 46-49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)	
1) ☐ Notice of References Cited (PTO-892)	4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)	5) ☐ Notice of Informal Patent Application
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/28/11*.	6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of Applicant's Request for Continued Examination filed on 04/05/2011; Amendment and Information Disclosure Statement filed on 03/28/2011.

- Claims 29-34, 38, 45-48 have been amended.
- Claim 49 has been added.
- Claim 41 has been cancelled.
- Claims 29-40, 42-49 are pending in the instant application.
- Claims 44-45 have been previously withdrawn from consideration.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 04/05/2011 has been entered.

Election/Restrictions

Applicant argues that the examiner states that claims 44 and 45 have been withdrawn from consideration because they lack unity with the invention originally claimed. The only ground that the examiner gives for this statement is that the originally presented claims pertain to composition claims only whereas claims 44 and 45 pertain

to method claims. The examiner states that it is irrelevant that the present case is subject to unity of invention practice because election by original presentation also applies to unity of invention practice. This restriction requirement is respectfully traversed. It is significant that the present application is subject to unity of invention practice as the examiner cannot rely upon election by original presentation unless the newly added claims lack unity of invention with the originally claimed invention. Here, the newly added claims do not lack unity of invention with the originally presented claims. The fact that the originally presented claims pertain to composition claims whereas claims 44 and 45 pertain to methods for use of the composition, does not automatically mean that they lack unity of invention. To the contrary, the examiner's attention is invited to 37 CFR §1.499, which states that the examiner can only find lack of unity of invention in a national stage application under the requirements of 37 CFR §1.475. 37 CFR §1.475(b)(2) states:

> [A] national stage application containing claims to different categories of invention will be considered to have unity of invention if the claims are drawn only to one of the following combinations of categories:
>
> (2) A product and process of use of said product ...

Accordingly, it is very clear according to the applicable regulations that a product and a process of use share unity of invention. The fact that the composition was elected by original presentation does not change the fact that the method of use of that composition shares unity of invention therewith and cannot be considered to be a separate invention that was not elected. Accordingly, reconsideration and withdrawal of

this unity of invention requirement and action on all of the claims now present in the case are respectfully urged.

The Examiner finds this argument unpersuasive, because claim 45 does not pertain to a "process of use of said product". Claim 45 pertains to "a process specially adapted for the manufacture of the said product". 37 CFR §1.475 further states in section (c) "If an application contains claims to more or less than one of the combinations of categories of invention set forth in paragraph (b) of this section, unity of invention might not be present" and (d) "If multiple products, processes of manufacture or uses are claimed, the first invention of the category first mentioned in the claims of the application and the first recited invention of each of the other categories related thereto will be considered as the main invention in the claims", in this instance, the only first recited invention of each categories was "a product".

Claim Rejections - 35 USC § 112, 1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 47 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claim is rejected because they do not identify the structure, material, or acts set forth in the specification that would be capable of carrying out the functional properties recited in the claims, such as "dissolution specifications". It appears from the specification that these claimed functional properties are achieved from specific formulations that contain specific ingredients, such as polyvinylpyrrolidone, ethylcellulose and dibutyl sebacate (see Examples). This is also evident by Applicant's arguments filed on 08/18/2010 that the prior art HEILIGENSTEIN having all the ingredients, such as hydrophilic polymer (hydroxypropyl methylcellulose), hydrophobic polymer (HPMACS, which is a cellulose acetate), and plasticizer, but failed to meet the equivalent of the "dissolution specifications". Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See In re Van Geuns, 988 F.2d 1181,26 USPQ2d 1057 (Fed. Cir. 1993). Accordingly, the ingredients, which make up the formulation, must be clearly and positively specified in order to place one of skill in the art in possession of the claimed tablets with the desired properties. It is precisely these ingredients that determines the desired properties and without which, one could not replicate the invention.

Applicant argues that Claim 47 has now been amended to specify the preferred components of the various layers. Furthermore, the reference to whether the layer is hydrophilic or hydrophobic is no longer relevant in light of specifying the ingredients, so this language has been deleted in favor of a functional description, i.e., "isolating layer" and "controlled release polymer." Thus, this claim now specifies that the active principle is venlafaxine hydrochloride and the pharmaceutical has three layers. A nonpareil inert

core is coated with the venlafaxine hydrochloride, which is optionally connected to a binder in an amount of 0.5 to 10 weight percent. The claim goes on to state that the second layer is an isolating layer, specifying the particular possible components of this layer, which layer comprises 0.5 to 10% based on the total weight of the dosage form. The claim further specifies that the outer layer is a controlled release layer comprising a controlled release polymer mixed with a plasticizer and specifying the possible components for the controlled release polymer, the controlled release polymer comprising 2-15 weight percent and the plasticizer being present in 0.1 to 2 weight percent. The claim then specifies that the parameters are selected so as to control release of the venlafaxine hydrochloride so as to obtain the desired pH- and rpm-independent in vitro dissolution specifications. The examiner has conceded on pages 4 and 5 of the Office action that it appears from the specification that the claimed functional properties are achieved from specific formulations that contain specific ingredients and that it is precisely these ingredients that determine the desired properties and without which one would not replicate the invention. As the specific ingredients from the specification are now claimed, the claims as presently amended are fully supported by the application as filed. Accordingly, the written description is sufficient to support the claim as presently amended.

The Examiner finds this argument unpersuasive, because Applicant's recited additional ingredients in a Markush group that would make the critical ingredients optional. For instance, Applicant's isolating layer can be hydroxypropyl methylcellulose, which is a hydrophilic polymer, and the controlled release layer can be hydroxypropyl

methylcellulose, which is a hydrophilic polymer, wherein no example in Applicant's specification shows this combination. Additionally, the use of hydroxypropyl methylcellulose as a controlled release layer is only possible with the combination of ethylcellulose (see Specification, Example 1-2).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 29-40, 42, 43, 46-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over HEILGENSTEIN (EP 0919236).

HEILIGENSTEIN teaches a composition comprised of: an active compound, such as venlafaxine hydrochloride (see pg. 3, line 8-9; pg. 4, line 48; and claim 2); a binder, such as hydroxypropyl methylcellulose (see pg. 3, line 33); a nonpareil inert core, such as sucrose (see pg. 3, line 28), which is an inert sugar; a separating layer (see pg. 3, line 34) made of hydrophilic polymers, such as hydroxypropyl methylcellulose (see pg. 3, line 35); a controlled release polymeric layer made of a cellulose acetate, such as HPMCAS (see pg. 3, line 39) or HPMC; and a plasticizer, such as triethyl citrate (see pg. 3, line 42). Additional disclosure includes: administering once a day (see pg. 4, line 48).

The reference does not specifically teach adding the ingredients in the amounts claimed by Applicant. The amount of a specific ingredient in a composition is clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ and reasonably would expect success. It would have been customary for an artisan of ordinary skill to determine the optimal amount of each ingredient to add in order to best achieve the desired results of the drug release over a specific time. Thus, absent some demonstration of unexpected results from the claimed parameters, this optimization of ingredient amount would have been obvious at the time of Applicant's invention.

Note, the prior art's composition is inherently capable of meeting the limitation of "wherein said layers cause the venlafaxine hydrochloride to be released over an approximately 24 hour period after oral administration" since the prior art's composition has the same ingredients, such as a separating layer (see pg. 3, line 34) made of hydroxypropyl methylcellulose (see pg. 3, line 35); a controlled release polymeric layer made of a cellulose acetate, such as HPMCAS (see pg. 3, line 39) or HPMC; and a plasticizer, as claimed by Applicant.

Claims 29-40, 42, 43, 46-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over OSHLACK et al (US 5,472,712) in view of SHERMAN (EP 0797991) and PALOMA COLL (US 5,232,706) as evidence by FDA (Guidance for Industry.

Bioavailability and bioequivalence studies for orally administered drug products - General considerations (2002)).

Applicant's claims are directed to an extended-released drug composition comprising of: a drug, such as venlafaxine hydrochloride, coated on a nonpareil inert sugar core; a binder, such as hydroxypropyl methylcellulose; a hydrophilic polymeric layer coating functioning as a separation layer, such as polyvinyl pyrrolidone or hydroxypropyl methylcellulose; a hydrophobic polymer, such as ethylcellulose; a plasticizer, such as dibutyl sebacate.

OSHLACK teaches an extended-released drug composition comprised of: a psychotropic drug (see col. 14, line 29), coated on nu pariel 18/20 beads (see col. 9, line 31-49; and col. 3, line 2-7), which reads on nonpareil inert sugar core; a binder, such as hydroxypropyl methylcellulose (see col. 9, line 50-55); a barrier layer (see col. 9, line 58-64), which reads on a hydrophilic polymeric layer coating functioning as a separation layer, such as hydroxypropyl methylcellulose or any film-former known in the art may be used (see col. 9, line 58-64); a hydrophobic polymer, such as ethylcellulose (see Title; col. 7, line 60-65; and col. 10, line 3) for controlling the drug release rate (see col. 2, line 13-17); a plasticizer, such as dibutyl sebacate (see col. 7, line 53 – col. 8, line 43, especially at col. 8, line 37-38). Additional disclosure includes: plasticizer will further improve the physical properties of the hydrophobic polymer film; rate-modifying agents, such as hydroxypropyl methylcellulose (see col. 11, line 53-65); therapeutic effect for about 24 hours (see col. 4, line 60-61); controlled release profile of the invention can be altered by varying the amount of ingredients or thickness of coating

(see col. 9, line 23-30; and col. 10, line 59-61); provides stabilized dissolution of the active agent for FDA approval (see Abstract; and col. 3, line 25-34; col. 5, line 25-30) .

OSHLACK does not teach using a drug, such as venlafaxine hydrochloride; or a separation layer, such as polyvinyl pyrrolidone.

SHERMAN teaches a 24 hour-extended release composition comprised of: a psychotropic drug, such as venlafaxine hydrochloride (see abstract), wherein a film-coating of ethylcellulose (see pg. 3, line 26) similar to OSHLACK is used to retard dissolution for extended release (see pg. 2, line 19) of the drug to reduce level of nausea and incidence of emesis that attend the administration of multiple daily dosing (see pg. 2, line 55-56).

PALOMO COLL teaches that separation layers made from hydroxypropyl methylcellulose and polyvinyl pyrrolidone are well known in the art (see co. 3, line 4-12).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to incorporate venlafaxine a drug, such as venlafaxine hydrochloride into OSHLACK's composition. The person of ordinary skill in the art would have been motivated to make those modifications, because it would improve the stability of the venlafaxine composition and still have 24-hour extended release of the drug to reduce level of nausea. The person of ordinary skill in the art reasonably would have expected success because OSHLACK and SHERMAN both dealt in the same field of endeavor, such as 24-hour extended-release formulations, and used the same film coating of ethylcellulose to control the dissolution rate of the drug.

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to incorporate a separation layer, such as polyvinyl pyrrolidone, into OSHLACK's composition. The person of ordinary skill in the art would have been motivated to make those modifications and reasonably would have expected success, because polyvinyl pyrrolidone and hydroxypropyl methylcellulose are functional equivalents used as separation layers in drug formulation, and OSHLACK teaches any film-form known in the art maybe used.

The references do not specifically teach adding the ingredients in the amounts claimed by Applicant. The amount of a specific ingredient in a composition is clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ and reasonably would expect success. It would have been customary for an artisan of ordinary skill to determine the optimal amount of each ingredient to add in order to best achieve the desired results, such as drug release rate to meet the requirement of the Food and Drug Administration approval for generic drug to be bioequivalent by dissolution studies to the reference drug, which is EFFEXOR XR in this case (if needed see FDA at pg. 1-2, 5-6 and 10-11). Thus, absent some demonstration of unexpected results from the claimed parameters, this optimization of ingredient amount would have been obvious at the time of Applicant's invention.

Note, one of ordinary skill in the art is well versed in FDA regulation for generic drug approval.

Response to Arguments

Applicant argues that the claims have now been amended to add a "wherein" clause at the end specifying that the layers cause the venlafaxine hydrochloride to be released "in a pH-independent manner over an approximately 24 hour period after oral administration." Thus, this important distinction over Heiligenstein is now in the claim and not merely in the preamble. Furthermore, the claims have been amended in order to specify the preferred components of the isolating layer as well as the controlled release polymer layer. The examiner has clearly taken the position at the first two lines of page 5 of the Office action that it is precisely these ingredients that determines the desired properties and without which, one could not replicate the invention. Thus, the present claims clearly define over Heiligenstein and would not be obvious therefrom, either alone or in combination with any other art of record.

The Examiner finds this argument unpersuasive, because as discussed above, HEILIGENSTEIN is inherently capable of meeting the limitation of "wherein said layers cause the venlafaxine hydrochloride to be released over an approximately 24 hour period after oral administration" since the prior art's composition has the same ingredients, such as a separating layer (see pg. 3, line 34) made of hydroxypropyl methylcellulose (see pg. 3, line 35); a controlled release polymeric layer made of a cellulose acetate, such as HPMCAS (see pg. 3, line 39) or HPMC; and a plasticizer, such as triethyl citrate (see pg. 3, line 42), as claimed by Applicant.

Applicant argues that it is well known in the art that the formulation of venlafaxine is particularly difficult because of its extremely high solubility and the existence of what is known as the "burst effect" or "burst phenomenon" (see the detailed discussion and supporting evidence below). Because of these special problems, those of ordinary skill in the art would not consider that standard techniques, such as those described by Oshlack that are used for the formulation of water insoluble or slightly water soluble pharmaceuticals, will necessarily solve the problems of obtaining extended release formulations of venlafaxine.

The Examiner finds this argument unpersuasive, because OSHLACK does not teach away from using venlafaxine. OSHLACK actually states that water-soluble drugs can be incorporated into the composition (see col. 14, line 10-11).

Applicant argues that after the effective filing date of the present invention, several groups around the world have filed patent applications attempting to resolve the problems of formulating venlafaxine into an extended release formulation. Some of these actually have derived solutions very similar to that of the present invention, but all of them considered their solutions to be sufficiently novel to warrant the filing of patent applications. All foreign patents and non-patent literature referred to below are being submitted on even date herewith to serve as evidence supporting the arguments for non-obviousness.

The Examine finds this argument unpersuasive, because venlafaxine was a patented drug under the trade name of "EFFEXXOR", wherein filing patents pertaining to venlafaxine would have been illegal, except for the patent holder, until the expiration

of the venlafaxine patent. Once the patent expired, then generic companies try to patent venlafaxine composition to prevent other companies from entering the venlafaxine market.

Applicant argues that there is nothing in any of the references of record which would suggest that the barrier coating of Palomo Coll would necessarily be useful in solving the burst phenomenon, which is a well-known problem when attempting to make extended release formulations of venlafaxine hydrochloride.

The Examiner finds this argument unpersuasive, because nothing in Applicant's specification shows that the isolation layer is absolutely necessary to prevent the burst phenomenon. For instance, Applicant's example 1-4 does not contain a separation/isolation/barrier coating. The only example that has this is example 5.

Telephonic Inquiries

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JAKE VU whose telephone number is (571)272-8148. The examiner can normally be reached on Mon-Tue and Thu-Fri 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jake M. Vu/
Primary Examiner, Art Unit 1618